

**A small change for man, a giant pain to
germkind!**



**An ingenious approach for detecting
pathogenic fungi.**



Here and again, iGEM 2014

Another year has gone by, and it is time for the next round of the iGEM competition. As before, a group of enthusiastic Masters Students (here at the Georg-August University of Göttingen), predominantly from the Life Science background have gathered to face the challenges.



iGEM is an international competition, developed and promoted by the Massachusetts Institute of Technology (MIT), situated in Cambridge in the United States of America. It stands for “International Genetically Engineered Machines”. It was established with the intention of bringing together the innovative synthetic biology and the importance of making the public aware in this emerging field of biology. In addition, it encourages the participants to come up with novel models and systems in the field of Synthetic Biology which will then be added to an ever growing collection of “Bio-Bricks”. This database will be available to future participants, thereby enabling the bio-bricks to become instrumental in the advancement of its own applications. The iGEM organization promotes the advancement of science and education by developing an open community of students and practitioners in

schools, laboratories, research institutes and industry.

In the last two years, the Georg-August University of Göttingen has been participating in this competition. With an increase in both quality and quantity of participants over the years from across the globe, iGEM has emerged to be one of the most sought after competition titles for both High School and University level students. On average more than 200 teams from all over the world participate in this event. This year is of special importance to iGEM: it is the 10th anniversary of this competition which started in 2004.

About the Team

Our iGEM team of 2014 has been in touch with the team from the previous year and they presented us the essentials of the competition, gave us pointers as to what we can do differently (or focus on) and most importantly, they encouraged us to carry their legacy forward.

The current team was assembled and finalized after numerous meetings. We decided on a topic that does justice to both the needs of the competition as well as benefit to humanity. We organized several meetings with professors from different departments of the Life Science groups at the University. Ultimately, we were able to reach a consensus regarding which area we will focus on. Our team is under the supervision of Prof. Dr. Gerhard Braus, Dr. Christoph Sasse (both from the Dept. of Molecular Microbiology and Genetics), and Dr. Joachim Uhrig (Department of Plant molecular Biology and Physiology).



Current state of pathogenic fungal detection

Today more than 300 million people suffer from problems like long term illness and blindness caused by fungal infections. This can even lead to death (www.life-worldwide.org).

The mold *Aspergillus fumigatus* is one of the most important human pathogenic fungi that cause severe aspergillosis in immunocompromised patients, leading to a mortality rate from 30-85%. Early diagnosis is critical for a favorable outcome, but is difficult to achieve with current methods. Until now, a range of alternative diagnostic strategies have been investigated but there is no simple method for diagnosis of invasive aspergillosis or invasive fungal infections in general. There is always the necessity to combine different procedure, since a single method is often not enough.



Figure 1: *Aspergillus fumigatus* grown by laboratory conditions. (Picture: Dr. David Midgley)

The established diagnostic procedures present for pathogenic fungal infections have certain disadvantages. Conventional diagnosis, which include the cultivation of fungi over days, is often very ineffective. This time consuming approach is in the majority of cases critical for the patients. Secondly, due to the delay in the appearance of fungal detection markers in body fluids (sputum, cerebrospinal fluid, blood, etc.), diagnosis of the disease is possible only at advanced stages. Finally, serious fungal infections in the body are not easily accessible to perform invasive diagnostic procedures.

An early diagnosis is associated with an increased patient survival rate. But since there is no standardized, fast diagnostic technique for invasive fungi, people are still dying from this kind of curable infection. For these reasons a range of different diagnostic strategies have been investigated. However, deep tissue diagnostic specimens are often difficult to obtain from critically ill persons. That is one of the reasons why a faster and simple method to detect fungal infection is needed.

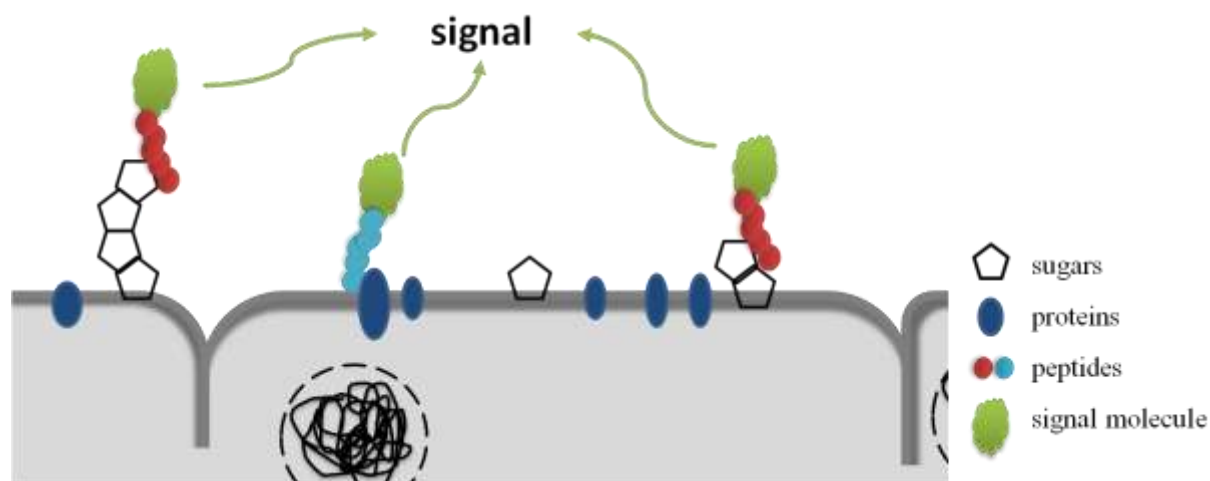


Figure 2: Model of fungal recognition by small peptide sequences. A fungal cell with the cell wall containing proteins and sugars is shown here. These surface molecules can be used as targets for detection and labeling. The different peptide sequences are able to bind to specific sugars or proteins of fungal species. These short peptide sequences can be linked to a fluorescent molecule (easy detection) or epitopes, which are recognized by macrophages (quick immune response).

Our Project

We intend to develop a fast screening technique for different invasive fungi, such as *Aspergillus fumigatus*, *Candida albicans* and *Aspergillus nidulans*. The idea is to tag the invasive fungal cells with a special protein marker, that allows an easy detection of fungi. By modifying the protein marker with a proper signal molecule, we will be able to accomplish a fast and direct detection or elimination of invasive fungi. This would avoid adverse effects and difficult, time-consuming diagnostic techniques.

On the surface of the previously mentioned fungi are many identical proteins and molecules but each species can have special ones that are unique for them.

Firstly we have to identify interactions between specific surface proteins of fungi and different protein markers (see figure 2). In a second step, this protein marker can be attached to different signal molecules. These could be proteins that produce detectable light or

proteins that can be recognized by immune cells. We are confident that this leads to an effective detection method and allows defeating invasive fungal infections.

Human impact – another aspect to be considered

Our project implies more than laboratory work and tackling challenges. We want to make synthetic biology and our project more charitable. The iGEM foundation called this part “human practices” in which creativity is important! People that are not in contact with science every day and the majority of non-biologist students do not know what is happening in laboratories. Our aim is to familiarize more people with laboratory work, synthetic biology and in the end our project.

We have started a video diary from the beginning that will last till the end of our project. A Facebook page and a homepage will also present our ideas.

Furthermore, there are a lot of additional ideas to enlarge the human practice part, for example a radio interview, news paper articles or a public event including a lottery. With this we hope to reach the general public awareness.

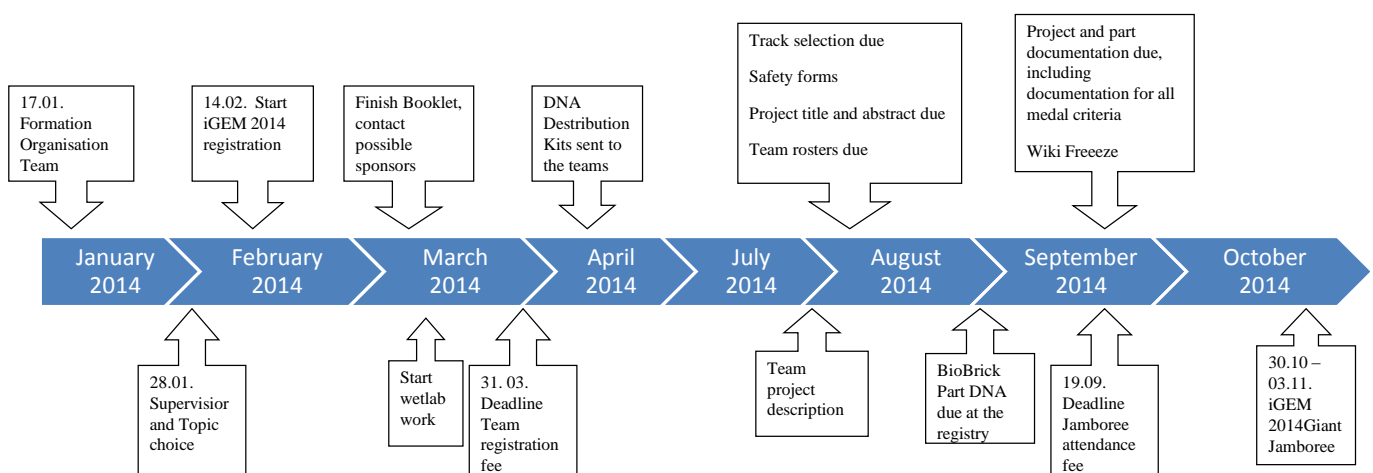
Budget

To have an idea how expensive this experience is, we set up a budget plan. The table beside catch up all possible expense items on our way. The only thing not included is the necessity that we have to get visa or ESTA for the entry to US.

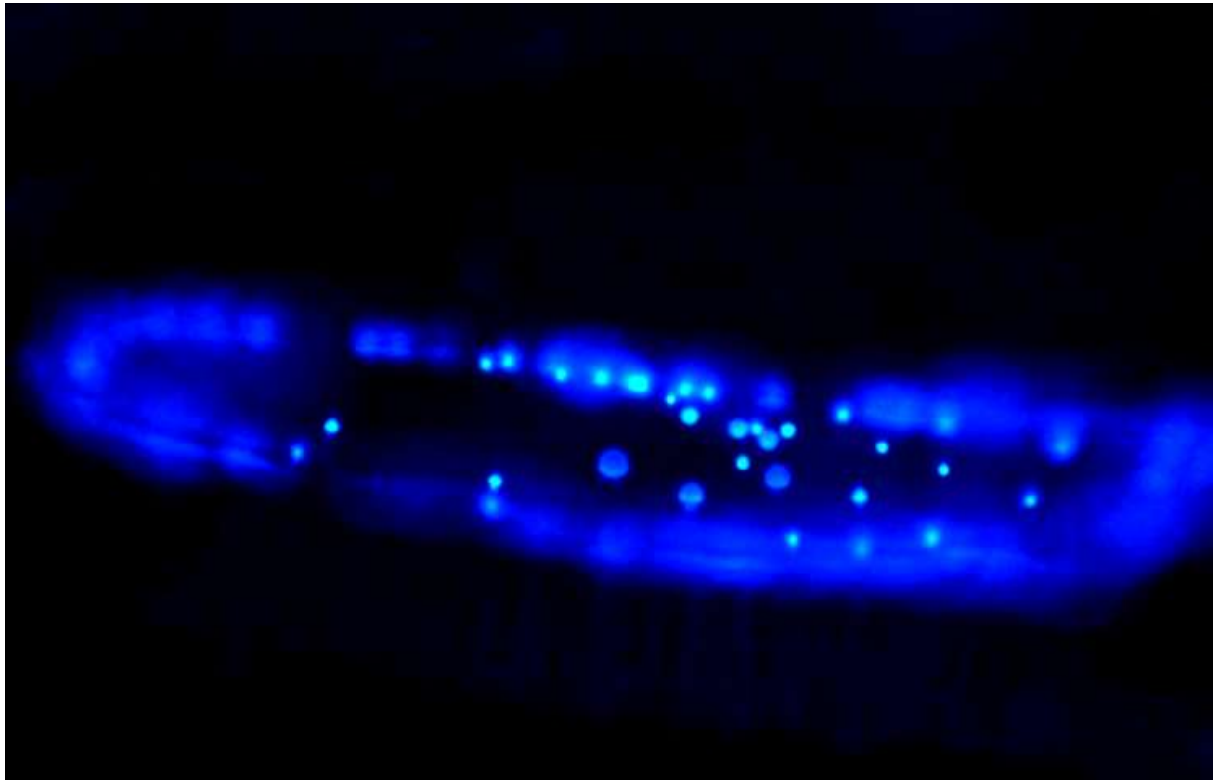
Expense item	Amount in \$	Amount in €
Team registration	3.500	2.554
Personal registration	15.000	10.944
Flight		12.525
Train		1.000
Accommodation	4.949	3.600
Promotion		2.500
Laboratory utilities		18.000
Total		51.123

Time schedule

This graphic should illustrate the important data on our way to the giant jamboree in Boston at the end of October 2014. There are more deadlines in our internal timer, but the official milestones are listed.



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